

What is claimed is:

1. A method of producing humanized or human antibodies comprising:

(a) treating a transgenic non-human animal in which rearrangement of immunoglobulin genes substantially stops early in life, engineered to express one or more human immunoglobulin loci, with at least one antibody specific for the surface IgM and/or IgD heavy and/or light chains produced by early B cells, whereby early B cells expressing said surface IgM and/or IgD heavy chains are depleted, and

(b) expressing said humanized or human immunoglobulin loci in said

2. The method of claim 1 wherein said animal relies substantially on gene conversion and/or other mutational processes to create primary antibody diversity.

3. The method of claim 1 wherein said animal substantially stops antibody diversification by gene rearrangement within the first month of its life.

1 4. The method of claim 1 wherein said animal is selected from the group
2 consisting of rabbits, birds, cows, pigs, sheep, goats and horses.

1 5. The method of claim 4 wherein said animal is selected from the group
2 consisting of rabbits, birds, cows and pigs.

1 6. The method of claim 5 wherein said animal is a transgenic rabbit or a
2 transgenic chicken expressing humanized or human immunoglobulin transgenes

1 7. The method of claim 1 wherein said antibody is a polyclonal antibody
2 preparation

1 8. The method of claim 7 wherein said polyclonal antibody preparation
2 comprises antibody fragments

1 9. The method of claim 7 wherein said polyclonal antibody preparation is
2 injected into said animal during embryonic life or the first weeks of life.

1 10. The method of claim 7 wherein said polyclonal antibody preparation is
2 injected into said transgenic animal during the first two weeks of its life.

1 11. The method of claim 7 wherein said polyclonal antibody preparation is
2 injected into said transgenic animal during the first month of its life.

1 12. The method of claim 1 wherein said antibody is a monoclonal antibody.

1 13. The method of claim 12 wherein said antibody is an antibody fragment.

1 14. The method of claim 11 wherein more than one monoclonal antibody is
2 administered.

1 15. The method of any one of claims 1, 7, 8, 12 and 13, wherein said antibody
2 is conjugated to a toxin to form an immunotoxin.

1 16. A method for suppressing endogenous immunoglobulin expression in a
2 non-human animal comprising expressing in said animal one or more transgenes
3 encoding one or more antibodies specific for the endogenous surface IgM and/or IgD
4 heavy and/or light chains produced by early B cells of said non-human animal.

1 17. The method of claim 16 wherein said animal is a transgenic animal
2 expressing a human or humanized antibody.

1 18. The method of claim 17 wherein said transgenic animal is a non-rodent
2 animal.

1 19. The method of claim 18 wherein said non-rodent transgenic animal relies
2 substantially on gene conversion and/or other non-templated mutational processes to
3 create primary antibody repertoires.

1 20. The method of claim 18 wherein said transgenic non-rodent animal
2 substantially stops antibody diversification by gene rearrangement early in life.

1 21. The method of claim 20 wherein said transgenic non-rodent animal
2 substantially stops antibody diversification by gene rearrangement within the first month
3 of its life.

1 22. The method of claim 18 wherein said non-rodent transgenic animal is
2 selected from the group consisting of rabbits, birds, cows, pigs, sheep, goats and horses.

1 23. The method of claim 22 wherein said non-rodent transgenic animal is
2 selected from the group consisting of rabbits, birds, cows and pigs.

1 24. A method for producing a non-human, non-rodent transgenic animal in
2 which endogenous immunoglobulin production is suppressed, comprising treating said
3 non-human, non-rodent transgenic animal with at least one antibody specific for the
4 endogenous surface IgM and/or IgD heavy and/or light chains produced by early B cells
5 of said animal.

1 25. A method for producing a non-human transgenic animal in which
2 endogenous immunoglobulin production is suppressed, comprising expressing in said
3 non-human transgenic animal one or more transgenes encoding one or more antibodies
4 specific for the endogenous surface IgM and/or IgD heavy and/or light chains produced
5 by early B cells of said animal.

1 26. A non-human transgenic animal dominantly expressing human or
2 humanized antibodies, wherein said animal (1) uses primarily gene conversion and/or
3 other mutational processes to diversify the primary antibody repertoire; (2) expresses a
4 transgene comprising a human immunoglobulin gene or an immunoglobulin gene of said
5 animal modified to express at least part of a human immunoglobulin molecule, and (3)
6 expresses a transgene coding for one or several antibodies specific for endogenous
7 surface IgM and/or IgD heavy and/or light chains produced by early B cells of said
8 animal

1 27. The non-human transgenic animal of claim 26 which expresses one or
2 several transgenes coding for one or several monoclonal antibodies capable of
3 suppressing production of endogenous immunoglobulin μ or δ heavy and/or light chains.

1
2 28. The non-human transgenic animal of claim 26 selected from the group
3 consisting of rabbits, birds, sheep, goat, pigs, cows and horses.